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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,116	10/23/2001	Henry Lamparski	348022000501	3354

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EXAMINER	
VOGEL, NANCY S	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 01/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,116	LAMPARSKI ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36 and 43-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36 and 43-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 36 and 43-52 are pending in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification as originally filed does not provide support for the invention as now claimed: "The adenovirus vector of Claim 36, further comprising a transgene encoding GM-CSF, operatively linked to a TRE other than a CEA-TRE" or "further comprising a transgene encoding a herpes simplex gene encoding thymidine kinase (HSV-tk) operatively linked to a TRE other than a CEA-TRE". This a new matter rejection. The specification does not provide sufficient blazemarks nor direction for the instant vectors encompassing the above-mentioned limitations, as currently recited. The instant claims now recite limitations which were not

clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112. It is noted that applicant has not pointed to any particular portion of the specification which provides support for the newly added claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 43-45 recite the limitation "said CEA enhancer" or "said CEA promoter" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim on which they depend, ie. claim 36. Furthermore, the claims are vague and indefinite since it cannot be determined whether the vectors recited therein are intended to contain the "polynucleotide sequence within about –402 to about +69 nucleotides relative to the transcriptional start site of the CEA gene" as recited in claim 36.

Claims 46-47 are vague and indefinite in the recitation of "said TRE consists essentially of a polynucleotide sequence from about -14.5 to about -10.6 kilobases relative to the transcriptional start site of the CEA gene" and "said CEA-TRE consists essentially of a polynucleotide sequence within the region from about -13.6 to about -

10.6 kilobases relative to the transcriptional start site of the CEA gene", since claim 36 on which the claims depend also recites a "polynucleotide sequence within about –402 to about +69 nucleotides relative to the transcriptional start site of the CEA gene". It is not clear if this polynucleotide sequence is intended to be included in the vectors recited in claims 46 and 47 since they recite the words "consisting essentially of" which would appear to exclude the –402 to +69 region.

Claim Rejections - 35 USC § 103

Claims 36 and 43-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hallenbeck et al. (WO 96/17053) in view of Richards et al. (WO 95/14100).

This rejection is maintained essentially for the reasons made of record in the previous Office action, mailed 12/16/04, with slight alterations necessitated by applicant's amendments to the claims.

Hallenbeck et al. teaches a replication competent adenovirus vector comprising a gene required for replication is under the control of a tissue-specific regulatory sequence (page6, lines 14-25). The preferred vector is adenovirus and the gene can be E1A, E1B or any other gene essential for replication, such as E2-E4 (page 17, lines 2-15). The preferred promoter is the carcinoembryonic antigen (CEA) (page 10, lines 6-8). The regulatory sequence can be used to control more than one gene (Page 16, lines 12-23). In one embodiment, both E1A and E1B are linked to separate tissue-specific regulatory sequences (page 17, lines 5-6). Hallenbeck et al. teaches that the

vector may comprise heterologous genes such as the HSV-tk gene or the GM-CSF gene (pages 24-25).

Hallenbeck et al. does not teach a specific CEA-TRE comprising an enhancer from the region of –14.5 to –3.8 relative to the transcriptional start site of the CEA gene or specific sequences. However, Richards et al. teaches a human CEA-TRE which includes sequences identical to SEQ ID NO:1 of the present application and which is used to express heterologous genes in cells which express CEA (page 3). Particular fragments disclosed to be useful are the enhancers located at –14.5 to –10.6, -13.6 to –10.6 and –6.1 to –3.8 upstream of the transcriptional start site (page 3). All of the regions can be included in either orientation and in different combinations. It would have been obvious to one of ordinary skill in the art at the time the invention way made to make the adenovirus vector comprising a CEA-TRE as taught by Hallenbeck et al. and to use the particular sequences of a CEA-TRE disclosed by Richards et al., motivated by the teachings of Richards et al. that the disclosed CEA-TRE sequences are effective for high level expression of a heterologous gene to which they are operably linked.

Applicant's arguments submitted 7/6/05 have been considered but have not been found convincing.

Applicants have argued that while Hallenbeck et al. describes adenoviral vectors that comprising a gene essential for replication operably linked to a heterologous transcriptional regulatory sequence (TRE), but that the reference does not disclose the

particular CEA regulatory sequences of the current claims, and that Richards et al. discloses genes of interest under the control of CEA enhancer sequences, Richards et al. does not "describe or suggest the use of a TRE to control expression of adenoviral genes such that adenovirus can replicate resulting in selective cytolysis of a target cell". However, while it agreed that neither reference discloses the invention as claimed in the instant application, it is maintained the references taken in combination render the instant invention obvious. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Hallenbeck et al. certainly suggests the use of a variety of transcriptional regulatory sequences in the disclosed adenoviral vectors, and it would have been obvious to one of ordinary skill in the art to have utilized the CEA TRE elements disclosed by Richards, in the vectors as disclosed by Hallenbeck et al. Therefore, the rejection is maintained.

Response to Amendment

Any rejection of record in the previous action not addressed in this office action is withdrawn. There are no new grounds of rejection that were not necessitated by applicants' amendment and therefore, this action is final.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NANCY VOGEL, PH.D.
PATENT EXAMINER

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1/5/06